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FACTORS RELATING TO NICOTINE PHYSIO-CHEMISTRY AND RETENTION IN HUMAN SMOKERS

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Summary

It has been alleged that tobacco companies add ammonia forming compounds to cigarettes in order to increase smoke 'pH' and thereby control the delivery of nicotine to the smoker. Furthermore, some claim that the addition of ammonium salts to tobaccos has a similar effect as that of adding bicarbonate salts to cocaine to produce 'crack'.

However, it can be shown that ammonium salts are used only to improve mechanical and sensory aspects of the product. Furthermore the concept of smoke 'pH' is scientifically invalid, the proposed mechanism for controlling nicotine delivery to the smoker is contrary to experimental data and the claimed comparison with crack cocaine is false.

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Source: https://www.industrydocuments.ucsf.edu/docs/mnpj0001

INTRODUCTION

The anti-tobacco lobby has accused the Tobacco Industry of deceit and malpractice regarding the use of ammonium salts on some tobacco products.

In 1995, the issue became high profile when 'The Wall Street Journal' said "Tobacco firm shows how ammonia spurs delivery of nicotine"; the issue re-emerged in 1997 when New Scientist observed; "Get your fix! Ammonia in tobacco increases the uptake of nicotine. Cigarettes have more in common with crack cocaine than you might think!" The text went on: "New research has confirmed that adding ammonia to tobacco - a technique similar to that of free-basing cocaine - greatly increases the ability of nicotine to enter a smoker's bloodstream."

It is useful to examine this issue from a number of perspectives.

- Why the tobacco industry may use 'ammonium salts' on some products.
- The allegations and claims made by the anti-tobacco lobby.
- Ammonia in tobacco smoke.
- The validity of the concept of 'smoke pH'.
- The claimed analogy with crack cocaine.
- Experimental data on nicotine and particulate behaviour when smoke is inhaled.

AMMONIUM SALTS HAVE SPECIFIC USES ON TOBACCO

The tobacco industry may use ammonium salts for specific product improvement purposes and these uses have been in the public record as patent filings for over 25 years.

Firstly, they assist in the manufacture of reconstituted tobacco sheet by improving binding.

Secondly, they serve as combustion modifiers in tobacco paper allowing greater cigarette design flexibility.

Thirdly, they contribute to smoke flavour - an important factor, especially for the design of lower delivery products.

ANTI-TOBACCO LOBBY CLAIMS

It has been claimed, that ammonia addition to cigarettes increases their addictive potential, relies on certain 'articles of faith' - assertions which they appear to accept unquestioningly. These claims are:

- Nicotine is an addictive drug.
- The faster nicotine is absorbed the greater the 'addictive' effect.
- The primary mechanism for this process is activation of nicotinic receptors in the brain.

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It has also been claimed that the Tobacco Industry adds ammonia forming compounds to tobacco in order to increase 'smoke pH'. This increase, it is said, enhances the proportion of the volatile, unprotonated, free base form of nicotine - sometimes termed 'free nicotine'. It is alleged that we do this to increase nicotine deposition in the deep lung gas exchange areas (the alveoli) from where it travels quickly to the brain.

But what is the truth.

AMMONIA IN SMOKE

Firstly, it is alleged that adding ammonium salts to tobacco enhances smoke ammonia levels and it is claimed to be this ammonia gas, a 'strong' base, which changes smoke 'pH'. However, at levels of ammonium salts typically used there is no measurable change in smoke ammonia. (Table 1)

Table 1: Effect of Diammonium Phosphate at Typical Application Level on Nicotine, NFDPM, and Ammonia in Mainstream Smoke

Cigarette	Nicotine (mg)	NFDPM (mg)	Ammonia (ug)
Control	1.0	14	47
Control with DAP*	1.0	13	47
	(ISO: r 0.1)	(ISO: r 1)	(± 10%)

* diammonium phosphate at 0.25% (2.5% on tobacco sheet; sheet inclusion at 10%)

SMOKE 'pH'

'pH' is a measure of hydrogen ion concentration (or more correctly, activity) in a **dilute, aqueous, homogenous, solution at equilibrium.**

Yet smoke is none of these. It is a complex of vapour and particles with thousands of components; and certainly - **not at equilibrium**. Smoke is a dynamic system and especially so during inhalation into the lungs. Indeed, in 1967 it was said that the definition of pH would tend to preclude its use in defining an aerosol system. *(A. J. Sensabaugh Jr and R. H. Cundiff, A new technique for determining the pH of whole tobacco smoke, Tobacco Science, 25, 1967.)*

It follows that the concept of a 'pH' value for smoke is scientifically unsound.

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FREE BASING COCAINE - A FALSE ANALOGY

Next, consider the allegation that adding ammonia to tobacco is like adding a bicarbonate salt to cocaine (free-basing).

Firstly, crack users reportedly mix the pure cocaine salt with an approximately equal amount of 'bicarbonate' (50:50). Yet ammonium salts, when applied to tobacco products, are at much lower levels - certainly less than 1% by weight of the total cigarette.

Secondly, it is the pure hydrochloride salt of cocaine that is normally 'free-based' - the salt of a strong acid. However, nicotine in tobacco is loosely bonded to weak organic acids.

Thirdly, there is a definite reaction between cocaine hydrochloride and the bicarbonate to liberate volatile cocaine base. Compare this with the complex chemistry and physics within a burning cigarette - ammonium salts at typically used levels contribute little, if anything, to this.

Fourthly, it is virtually impossible to generate a smoke aerosol from cocaine hydrochloride alone. If cocaine hydrochloride is heated without bicarbonate present very little cocaine is produced. Bicarbonate is necessary to generate volatile cocaine when heat is applied. *(Y. Nakahara and A. Ishigami, Inhalation efficiency of free-base cocaine by pyrolyis of 'crack' and cocaine hydrochloride, J. Anal. Toxicol. 16, 1991.)*

In contrast, when tobacco is burnt, with or without ammonium salts present, distillation of volatile material readily takes place ahead of the burning cone with smoke particles being generated from the complex tobacco plant matrix.

The above demonstrates that there are fundamental differences between adding ammonium salts to tobacco and free-basing cocaine.

NICOTINE AND SOLANESOL RETENTION ON INHALATION

It is claimed that adding ammonium salts to tobacco increases the rate of nicotine transport from the respiratory tract to the brain. However, human experimental data on nicotine retention at progressive lung depths and the consequent blood nicotine levels suggests a different process.

Although the study described below used a product with no ammonium salts it will become apparent that the results are highly relevant.

The following pilot study was carried out at Rothmans International in order to obtain information on what happens to nicotine and smoke particles when inhalation depth is controlled?

The study involved 4 volunteers smoking their own (Virginia) brand. Solanesol, an involatile tobacco specific substance, was used as the surrogate analyte for 'tar'. Smoking behaviour (puffing dynamics) was recorded and the smoking occasions later 'duplicated' on a smoking machine to obtain nicotine and solanesol delivery to the mouth. Volunteers were asked not to let any smoke drift from their

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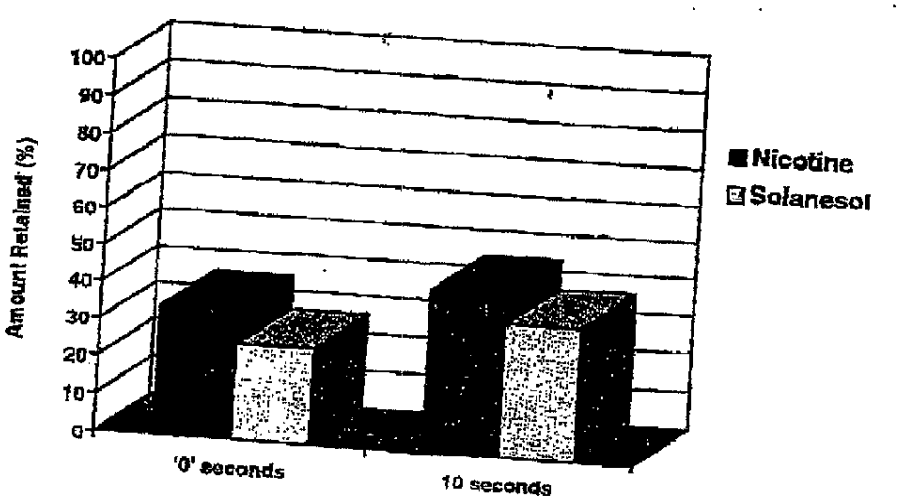
mouths prior to inhalation. Inhalation depth was the key variable. All exhaled smoke was collected and analysed for solanesol and nicotine and the nicotine and solanesol retained was expressed as a % of that generated.

Firstly we looked at taking smoke into the mouth and not inhaling.

When smoke was taken in and exhaled immediately, the 0 seconds example of Figure 1, about 35% of the available nicotine and about 25% of the solanesol was retained.

With a 10 second mouth hold the mouth retention for nicotine increased to 40% and solanesol increased to about 35%. (Figure 1).

Figure 1



The effect of 'depth of inhalation' after a normal puff is shown in Figure 2. With a shallow, 70 ml inhalation, over 80% of the nicotine was retained - most of this will be in the upper respiratory tract and not deep enough to penetrate the alveoli. It would be unavailable for rapid transport to the brain.

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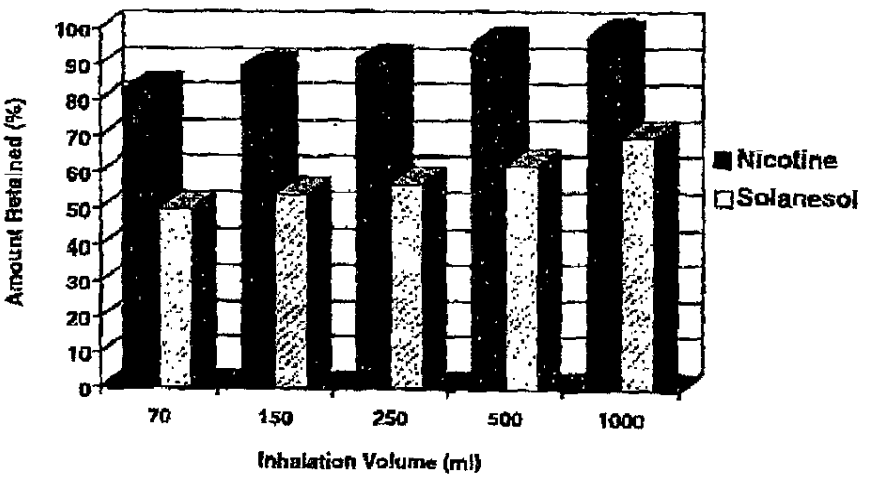
Figure 2



Also note that solanesol retention was much less at 50%. Indeed, exhaled particles were found to be virtually free of nicotine. It seems that nicotine evaporated from the particles within a second or so or inhaling.

Therefore it appears that even with an 'ammonium salt free' cigarette nicotine will evaporate rapidly from smoke particles before reaching the lung alveoli.

A typical smoker would normally inhale between about 500 ml and 700 ml. Figure 2 shows that over 90% of nicotine is retained after a 500 ml inhalation so even with the 'ammonium salt free' product, as used in this study, virtually all the available nicotine is retained. There is little scope here for increasing nicotine absorption at the alveolar level by use of additives such as ammonium salts.

It follows that any product change which might increase the speed at which nicotine evaporates from smoke particles would cause more nicotine to be released in the upper respiratory tract and so reduce alveolar exposure lower down.

This conclusion is supported by plasma nicotine levels obtained in a separate, but essentially identical study. Blood was sampled before smoking and 10 minutes after lighting - just after the cigarette was finished. The results are shown in Figure 3.

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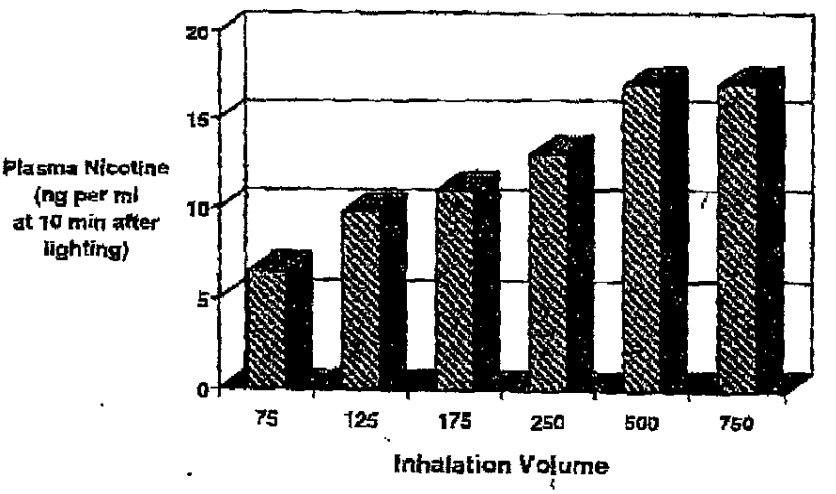
Figure 3



A 75 ml inhalation gave comparatively low levels of nicotine in blood whilst an inhalation of 500 ml, to the alveoli, produced a value three times higher. Compare this 3 fold increase for blood nicotine with essentially no increase for nicotine retention in Figure 2. The results show that with a 75 ml inhalation much of the retained nicotine does not appear in the plasma. It is proposed that with a shallow inhalation much nicotine is absorbed in the upper airways - rather than in the alveoli - and so very little reaches the brain before it is distributed in tissues and metabolized in the body as a whole. Thus a prediction from this study is that making smoke more alkaline would not increase nicotine transport to the brain - contrary to the claims in 'The Wall Street Journal' and 'New Scientist'. Indeed, if any technology were used on tobacco sufficient to increase significantly smoke ammonia levels then more nicotine would be deposited in the upper respiratory tract and less would go to the brain.

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CONCLUSIONS

1. Ammonium salts have specific uses in tobacco products.
2. Smoke ammonia levels are unaffected by typical ammonium salt levels on tobacco.
3. The idea of smoke having a measurable pH is scientifically unsound.
4. The analogy with free-basing cocaine is false.
5. Nicotine is significantly retained in the upper respiratory tract.
6. With a conventional cigarette nicotine retention after a normal inhalation is virtually 100%.
7. Making tobacco smoke more alkaline would not increase nicotine retention in the lower respiratory tract (alveoli). Indeed, the consequence would be to increase retention in the upper airways so reducing retention lower down and hence reducing nicotine transport to the brain.

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